



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Craig C. Mello et al.  
Serial No. : 09/689,992  
Filed : October 13, 2000  
Title : RNA INTERFERENCE PATHWAY GENES AS TOOLS FOR TARGETED GENETIC INTERFERENCE

Art Unit : 1656  
Examiner : T. Strzelecka

**BOX SEQUENCE**

Commissioner for Patents  
Washington, D.C. 20231

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I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of The United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Date: June 18, 2001

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JUN 26 2001

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## SEQUENCE LISTING

<110> Mello, Craig C.  
Tabara, Hiroaki  
Grishok, Alla  
Fire, Andrew

<120> RNA INTERFERENCE PATHWAY GENES AS TOOLS FOR TARGETED GENETIC INTERFERENCE

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<140> US 09/689,992

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<212> PRT

<213> *Caenorhabditis elegans*

<220>

<221> VARIANT

<222> (1)...(406)

<223> Xaa = Any Amino Acid

<400> 5

Met	Asp	Leu	Thr	Lys	Leu	Thr	Phe	Glu	Ser	Val	Phe	Gly	Gly	Ser	Asp
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Val	Pro	Met	Lys	Pro	Ser	Arg	Ser	Glu	Asp	Asn	Lys	Thr	Pro	Arg	Asn
			20					25					30		
Arg	Thr	Asp	Leu	Glu	Met	Phe	Leu	Lys	Lys	Thr	Pro	Leu	Met	Val	Leu
		35				40						45			
Glu	Glu	Ala	Ala	Lys	Ala	Val	Tyr	Gln	Lys	Thr	Pro	Thr	Trp	Gly	Thr
	50				55					60					
Val	Glu	Leu	Pro	Glu	Gly	Phe	Glu	Met	Thr	Leu	Ile	Leu	Asn	Glu	Ile
65					70					75				80	

Thr Val Lys Gly Gln Ala Thr Ser Lys Lys Ala Ala Arg Gln Lys Ala  
 85 90 95  
 Ala Val Glu Tyr Leu Arg Lys Val Val Glu Lys Gly Lys His Glu Ile  
 100 105 110  
 Phe Phe Ile Pro Gly Thr Thr Lys Glu Glu Ala Leu Ser Asn Ile Asp  
 115 120 125  
 Gln Ile Ser Asp Lys Ala Glu Glu Leu Lys Arg Ser Thr Ser Asp Ala  
 130 135 140  
 Val Gln Asp Asn Asp Asn Asp Asp Ser Ile Pro Thr Ser Ala Glu Phe  
 145 150 155 160  
 Pro Pro Gly Ile Ser Pro Thr Glu Asn Trp Val Gly Lys Leu Gln Glu  
 165 170 175  
 Lys Ser Gln Lys Ser Lys Leu Gln Ala Pro Ile Tyr Glu Asp Ser Lys  
 180 185 190  
 Asn Glu Arg Thr Glu Arg Phe Leu Val Ile Cys Thr Met Cys Asn Gln  
 195 200 205  
 Lys Thr Arg Gly Ile Arg Ser Lys Lys Lys Asp Ala Lys Asn Leu Ala  
 210 215 220  
 Ala Trp Leu Met Trp Lys Ala Leu Glu Asp Gly Ile Glu Ser Leu Glu  
 225 230 235 240  
 Ser Tyr Asp Met Val Asp Val Ile Glu Asn Leu Glu Glu Ala Glu His  
 245 250 255  
 Leu Leu Glu Ile Gln Asp Gln Ala Ser Lys Ile Lys Asp Lys His Ser  
 260 265 270  
 Ala Leu Ile Asp Ile Leu Ser Asp Lys Lys Arg Phe Ser Asp Tyr Ser  
 275 280 285  
 Met Asp Phe Asn Val Leu Ser Val Ser Thr Met Gly Ile His Gln Val  
 290 295 300  
 Leu Leu Glu Ile Ser Phe Arg Arg Leu Val Ser Pro Asp Pro Asp Asp  
 305 310 315 320  
 Leu Glu Met Gly Ala Glu His Thr Gln Thr Glu Glu Ile Met Lys Ala  
 325 330 335  
 Thr Ala Glu Lys Glu Lys Leu Arg Lys Lys Asn Met Pro Asp Ser Gly  
 340 345 350  
 Pro Leu Val Phe Ala Gly His Gly Ser Ser Ala Glu Glu Ala Lys Gln  
 355 360 365  
 Cys Ala Cys Lys Ser Ala Ile Ile His Phe Asn Thr Tyr Asp Phe Thr  
 370 375 380  
 Asp Lys Tyr Tyr Cys Val Phe Leu Lys Asn Glu Ala Ser Glu Xaa Leu  
 385 390 395 400  
 Xaa Lys Lys Lys Lys Lys  
 405

<210> 6

<211> 763

<212> PRT

<213> Arabidopsis thaliana

<400> 6

Gly Ile Ile Asn Gly Pro Lys Arg Glu Arg Ser Tyr Lys Val Ala Ile  
 1 5 10 15  
 Lys Phe Val Ala Arg Ala Asn Met His His Leu Gly Glu Phe Leu Ala  
 20 25 30  
 Gly Lys Arg Ala Asp Cys Pro Gln Glu Ala Val Gln Ile Leu Asp Ile  
 35 40 45  
 Val Leu Arg Glu Leu Ser Val Lys Arg Phe Cys Pro Val Gly Arg Ser  
 50 55 60



Phe Phe Ser Pro Asp Ile Lys Thr Pro Gln Arg Leu Gly Glu Gly Leu  
 65 70 75 80  
 Glu Ser Trp Cys Gly Phe Tyr Gln Ser Ile Arg Pro Thr Gln Met Gly  
 85 90 95  
 Leu Ser Leu Asn Ile Asp Met Ala Ser Ala Ala Phe Ile Glu Pro Leu  
 100 105 110  
 Pro Val Ile Glu Phe Val Ala Gln Leu Leu Gly Lys Asp Val Leu Ser  
 115 120 125  
 Lys Pro Leu Ser Asp Ser Asp Arg Val Lys Ile Lys Lys Gly Leu Arg  
 130 135 140  
 Gly Val Lys Val Glu Val Thr His Arg Ala Asn Val Arg Arg Lys Tyr  
 145 150 155 160  
 Arg Val Ala Gly Leu Thr Thr Gln Pro Thr Arg Glu Leu Met Phe Pro  
 165 170 175  
 Val Asp Glu Asn Cys Thr Met Lys Ser Val Ile Glu Tyr Phe Gln Glu  
 180 185 190  
 Met Tyr Gly Phe Thr Ile Gln His Thr His Leu Pro Cys Leu Gln Val  
 195 200 205  
 Gly Asn Gln Lys Lys Ala Ser Tyr Leu Pro Met Glu Ala Cys Lys Ile  
 210 215 220  
 Val Glu Gly Gln Arg Tyr Thr Lys Arg Leu Asn Glu Lys Gln Ile Thr  
 225 230 235 240  
 Ala Leu Leu Lys Val Thr Cys Gln Arg Ala Glu Gly Gln Arg Asn Asp  
 245 250 255  
 Ile Leu Arg Thr Val Gln His Asn Ala Tyr Asp Gln Asp Pro Tyr Ala  
 260 265 270  
 Lys Glu Phe Gly Met Asn Ile Ser Glu Lys Leu Ala Ser Val Glu Ala  
 275 280 285  
 Arg Ile Leu Pro Ala Pro Trp Leu Lys Tyr His Glu Asn Gly Lys Glu  
 290 295 300  
 Lys Asp Cys Leu Pro Gln Val Gly Gln Trp Asn Met Met Asn Lys Lys  
 305 310 315 320  
 Met Ile Asn Gly Met Thr Val Ser Arg Trp Ala Cys Val Asn Phe Ser  
 325 330 335  
 Arg Ser Val Gln Glu Asn Val Ala Arg Gly Phe Cys Asn Glu Leu Gly  
 340 345 350  
 Gln Met Cys Glu Val Ser Gly Met Glu Phe Asn Pro Glu Pro Val Ile  
 355 360 365  
 Pro Ile Tyr Ser Ala Arg Pro Asp Gln Val Glu Lys Ala Leu Lys His  
 370 375 380  
 Val Tyr His Thr Ser Met Asn Lys Thr Lys Gly Lys Glu Leu Glu Leu  
 385 390 395 400  
 Leu Leu Ala Ile Leu Pro Asp Asn Asn Gly Ser Leu Tyr Gly Asp Leu  
 405 410 415  
 Lys Arg Ile Cys Glu Thr Glu Leu Gly Leu Ile Ser Gln Cys Cys Leu  
 420 425 430  
 Thr Lys His Val Phe Lys Ile Ser Lys Gln Tyr Leu Ala Asp Val Ser  
 435 440 445  
 Leu Lys Ile Asn Val Lys Met Gly Gly Arg Asn Thr Val Leu Val Asp  
 450 455 460  
 Ala Ile Ser Cys Arg Ile Pro Leu Val Ser Asp Ile Pro Thr Ile Ile  
 465 470 475 480  
 Phe Gly Ala Asp Val Thr His Pro Glu Asn Gly Glu Glu Ser Ser Pro  
 485 490 495  
 Ser Ile Ala Ala Val Val Ala Ser Gln Asp Trp Pro Glu Val Thr Lys  
 500 505 510

Tyr Ala Gly Leu Val Cys Ala Gln Ala His Arg Gln Glu Leu Ile Gln  
 515 520 525  
 Asp Leu Tyr Lys Thr Trp Gln Asp Pro Val Arg Gly Thr Val Ser Gly  
 530 535 540  
 Gly Met Ile Arg Asp Leu Leu Ile Ser Phe Arg Lys Ala Thr Gly Gln  
 545 550 555 560  
 Lys Pro Leu Arg Ile Ile Phe Tyr Arg Asp Gly Val Ser Glu Gly Gln  
 565 570 575  
 Phe Tyr Gln Val Leu Leu Tyr Glu Leu Asp Ala Ile Arg Lys Ala Cys  
 580 585 590  
 Ala Ser Leu Glu Pro Asn Tyr Gln Pro Pro Val Thr Phe Ile Val Val  
 595 600 605  
 Gln Lys Arg His His Thr Arg Leu Phe Ala Asn Asn His Arg Asp Lys  
 610 615 620  
 Asn Ser Thr Asp Arg Ser Gly Asn Ile Leu Pro Gly Thr Val Val Asp  
 625 630 635 640  
 Thr Lys Ile Cys His Pro Thr Glu Phe Asp Phe Tyr Leu Cys Ser His  
 645 650 655  
 Ala Gly Ile Gln Gly Thr Ser Arg Pro Ala His Tyr His Val Leu Trp  
 660 665 670  
 Asp Glu Asn Asn Phe Thr Ala Asp Gly Ile Gln Ser Leu Thr Asn Asn  
 675 680 685  
 Leu Cys Tyr Thr Tyr Ala Arg Cys Thr Arg Ser Val Ser Ile Val Pro  
 690 695 700  
 Pro Ala Tyr Tyr Ala His Leu Ala Ala Phe Arg Ala Arg Phe Tyr Leu  
 705 710 715 720  
 Glu Pro Glu Ile Met Gln Asp Asn Gly Ser Pro Gly Lys Lys Asn Thr  
 725 730 735  
 Lys Thr Thr Thr Val Gly Asp Val Gly Val Lys Pro Leu Pro Ala Leu  
 740 745 750  
 Lys Glu Asn Val Lys Arg Val Met Phe Tyr Cys  
 755 760

<210> 7

<211> 678

<212> PRT

<213> *Drosophila melanogaster*

<400> 7

Arg Ala Gly Glu Asn Ile Glu Ile Lys Ile Lys Ala Val Gly Ser Val  
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 Gln Ser Thr Asp Ala Glu Gln Phe Gln Val Leu Asn Leu Ile Leu Arg  
 20 25 30  
 Arg Ala Met Glu Gly Leu Asp Leu Lys Leu Val Ser Arg Tyr Tyr Tyr  
 35 40 45  
 Asp Pro Gln Ala Lys Ile Asn Leu Glu Asn Phe Arg Met Gln Leu Trp  
 50 55 60  
 Pro Gly Tyr Gln Thr Ser Ile Arg Gln His Glu Asn Asp Ile Leu Leu  
 65 70 75 80  
 Cys Ser Glu Ile Cys His Lys Val Met Arg Thr Glu Thr Leu Tyr Asn  
 85 90 95  
 Ile Leu Ser Asp Ala Ile Arg Asp Ser Asp Asp Tyr Gln Ser Thr Phe  
 100 105 110  
 Lys Arg Ala Val Met Gly Met Val Ile Leu Thr Asp Tyr Asn Asn Lys  
 115 120 125  
 Thr Tyr Arg Ile Asp Asp Val Asp Phe Gln Ser Thr Pro Leu Cys Lys  
 130 135 140

Phe Lys Thr Asn Asp Gly Glu Ile Ser Tyr Val Asp Tyr Tyr Lys Lys  
 145 150 155 160  
 Arg Tyr Asn Ile Ile Ile Arg Asp Leu Lys Gln Pro Leu Val Met Ser  
 165 170 175  
 Arg Pro Thr Asp Lys Asn Ile Arg Gly Gly Asn Asp Gln Ala Ile Met  
 180 185 190  
 Ile Ile Pro Glu Leu Ala Arg Ala Thr Gly Met Thr Asp Ala Met Arg  
 195 200 205  
 Ala Asp Phe Arg Thr Leu Arg Ala Met Ser Glu His Thr Arg Leu Asn  
 210 215 220  
 Pro Asp Arg Arg Ile Glu Arg Leu Arg Met Phe Asn Lys Arg Leu Lys  
 225 230 235 240  
 Ser Cys Lys Gln Ser Val Glu Thr Leu Lys Ser Trp Asn Ile Glu Leu  
 245 250 255  
 Asp Ser Ala Leu Val Glu Ile Pro Ala Arg Val Leu Pro Pro Glu Lys  
 260 265 270  
 Ile Leu Phe Gly Asn Gln Lys Ile Phe Val Cys Asp Ala Arg Ala Asp  
 275 280 285  
 Trp Thr Asn Glu Phe Arg Thr Cys Ser Met Phe Lys Asn Val His Ile  
 290 295 300  
 Asn Arg Trp Tyr Val Ile Thr Pro Ser Arg Asn Leu Arg Glu Thr Gln  
 305 310 315 320  
 Glu Phe Val Gln Met Cys Ile Arg Thr Ala Ser Ser Met Lys Met Asn  
 325 330 335  
 Ile Cys Asn Pro Ile Tyr Glu Glu Ile Pro Asp Asp Arg Asn Gly Thr  
 340 345 350  
 Tyr Ser Gln Ala Ile Asp Asn Ala Ala Asn Asp Pro Gln Ile Val  
 355 360 365  
 Met Val Val Met Arg Ser Pro Asn Glu Glu Lys Tyr Ser Cys Ile Lys  
 370 375 380  
 Lys Arg Thr Cys Val Asp Arg Pro Val Pro Ser Gln Val Val Thr Leu  
 385 390 395 400  
 Lys Val Ile Ala Pro Arg Gln Gln Lys Pro Thr Gly Leu Met Ser Ile  
 405 410 415  
 Ala Thr Lys Val Val Ile Gln Met Asn Ala Lys Leu Met Gly Ala Pro  
 420 425 430  
 Trp Gln Val Val Ile Pro Leu His Gly Leu Met Thr Val Gly Phe Asp  
 435 440 445  
 Val Cys His Ser Pro Lys Asn Lys Asn Lys Ser Tyr Gly Ala Phe Val  
 450 455 460  
 Ala Thr Met Asp Gln Lys Glu Ser Phe Arg Tyr Phe Ser Thr Val Asn  
 465 470 475 480  
 Glu His Ile Lys Gly Gln Glu Leu Ser Glu Gln Met Ser Val Asn Met  
 485 490 495  
 Ala Cys Ala Leu Arg Ser Tyr Gln Glu Gln His Arg Ser Leu Pro Glu  
 500 505 510  
 Arg Ile Leu Phe Phe Arg Asp Gly Val Gly Asp Gly Gln Leu Tyr Gln  
 515 520 525  
 Val Val Asn Ser Glu Val Asn Thr Leu Lys Asp Arg Leu Asp Glu Ile  
 530 535 540  
 Tyr Lys Ser Ala Gly Lys Gln Glu Gly Cys Arg Met Thr Phe Ile Ile  
 545 550 555 560  
 Val Ser Lys Arg Ile Asn Ser Arg Tyr Phe Thr Gly His Arg Asn Pro  
 565 570 575  
 Val Pro Gly Thr Val Val Asp Asp Val Ile Thr Leu Pro Glu Arg Tyr  
 580 585 590

[illegible]

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<210> 8
<211> 23
<212> PRT
<213> Artificial Sequence
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<220>  
<223> Consensus sequence

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<400> 8
Pro  Leu  Glu  Gln  Tyr  Gly  Pro  His  Phe  Val  Gly  Gly  Gly  Ser  Lys  Lys
 1          5          10
Ala  Lys  Ala  Ala  Leu  Leu
          20

```

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<210> 9
<211> 766
<212> PRT
<213> Caenorhabditis elegans
```

<400> 9

Ser	Ala	Val	Glu	Arg	Gln	Phe	Ser	Val	Ser	Leu	Lys	Trp	Val	Gly	Gln
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Val	Ser	Leu	Ser	Thr	Leu	Glu	Asp	Ala	Met	Glu	Gly	Arg	Val	Arg	Gln
			20					25					30		
Val	Pro	Phe	Glu	Ala	Val	Gln	Ala	Met	Asp	Val	Ile	Leu	Arg	His	Leu
		35					40					45			
Pro	Ser	Leu	Lys	Tyr	Thr	Pro	Val	Gly	Arg	Ser	Phe	Phe	Ser	Pro	Pro
	50					55					60				
Val	Pro	Asn	Ala	Ser	Gly	Val	Met	Ala	Gly	Ser	Cys	Pro	Pro	Gln	Ala
65					70					75					
Ser	Gly	Ala	Val	Ala	Gly	Gly	Ala	His	Ser	Ala	Gly	Gln	Tyr	His	Ala
				85					90						
Glu	Ser	Lys	Leu	Gly	Gly	Gly	Arg	Glu	Val	Trp	Phe	Gly	Phe	His	Gln
			100					105					110		
Ser	Val	Arg	Pro	Ser	Gln	Trp	Lys	Met	Met	Leu	Asn	Ile	Asp	Val	Ser
		115					120					125			
Ala	Thr	Ala	Phe	Tyr	Arg	Ser	Met	Pro	Val	Ile	Glu	Phe	Ile	Ala	Glu
	130					135					140				
Val	Leu	Glu	Leu	Pro	Val	Gln	Ala	Leu	Ala	Glu	Arg	Arg	Ala	Leu	Ser
145					150					155					
Asp	Ala	Gln	Arg	Val	Lys	Phe	Thr	Lys	Glu	Ile	Arg	Gly	Leu	Lys	Ile
				165					170					175	
Glu	Ile	Thr	His	Cys	Gly	Gln	Met	Arg	Arg	Lys	Tyr	Arg	Val	Cys	Asn
			180					185						190	

Val Thr Arg Arg Pro Ala Gln Thr Gln Thr Phe Pro Leu Gln Leu Glu  
 195 200 205  
 Thr Gly Gln Thr Ile Glu Cys Thr Val Ala Lys Tyr Phe Tyr Asp Lys  
 210 215 220  
 Tyr Arg Ile Gln Leu Lys Tyr Pro His Leu Pro Cys Leu Gln Val Gly  
 225 230 235 240  
 Gln Glu Gln Lys His Thr Tyr Leu Pro Pro Glu Val Cys Asn Ile Val  
 245 250 255  
 Pro Gly Gln Arg Cys Ile Lys Lys Leu Thr Asp Val Gln Thr Ser Thr  
 260 265 270  
 Met Ile Lys Ala Thr Ala Arg Ser Ala Pro Glu Arg Glu Arg Glu Ile  
 275 280 285  
 Ser Asn Leu Val Arg Lys Ala Glu Phe Ser Ala Asp Pro Phe Ala His  
 290 295 300  
 Glu Phe Gly Ile Thr Ile Asn Pro Ala Met Thr Glu Val Lys Gly Arg  
 305 310 315 320  
 Val Leu Ser Ala Pro Lys Leu Leu Tyr Gly Gly Arg Thr Arg Ala Thr  
 325 330 335  
 Ala Leu Pro Asn Gln Gly Val Trp Asp Met Arg Gly Lys Gln Phe His  
 340 345 350  
 Thr Gly Ile Asp Val Arg Val Trp Ala Ile Ala Cys Phe Ala Gln Gln  
 355 360 365  
 Gln His Val Lys Glu Asn Asp Leu Arg Met Phe Thr Asn Gln Leu Gln  
 370 375 380  
 Arg Ile Ser Asn Asp Ala Gly Met Pro Ile Val Gly Asn Pro Cys Phe  
 385 390 395 400  
 Cys Lys Tyr Ala Val Gly Val Glu Gln Val Glu Pro Met Phe Lys Tyr  
 405 410 415  
 Leu Lys Gln Asn Tyr Ser Gly Ile Gln Leu Val Val Val Val Leu Pro  
 420 425 430  
 Gly Lys Thr Pro Val Tyr Ala Glu Val Lys Arg Val Gly Asp Thr Val  
 435 440 445  
 Leu Gly Ile Ala Thr Gln Cys Val Gln Ala Lys Asn Ala Ile Arg Thr  
 450 455 460  
 Thr Pro Gln Thr Leu Ser Asn Leu Cys Leu Lys Met Asn Val Lys Leu  
 465 470 475 480  
 Gly Gly Val Asn Ser Ile Leu Leu Pro Asn Val Arg Pro Arg Ile Phe  
 485 490 495  
 Asn Glu Pro Val Ile Phe Phe Gly Cys Asp Ile Thr His Pro Pro Ala  
 500 505 510  
 Gly Asp Ser Arg Lys Pro Ser Ile Ala Ala Val Val Gly Ser Met Asp  
 515 520 525  
 Ala His Pro Ser Arg Tyr Ala Ala Thr Val Arg Val Gln Gln His Arg  
 530 535 540  
 Gln Glu Ile Ile Ser Asp Leu Thr Tyr Met Val Arg Glu Leu Leu Val  
 545 550 555 560  
 Gln Phe Tyr Arg Asn Thr Arg Phe Lys Pro Ala Arg Ile Val Val Tyr  
 565 570 575  
 Arg Asp Gly Val Ser Glu Gly Gln Phe Phe Asn Val Leu Gln Tyr Glu  
 580 585 590  
 Leu Arg Ala Ile Arg Glu Ala Cys Met Met Leu Glu Arg Gly Tyr Gln  
 595 600 605  
 Pro Gly Ile Thr Phe Ile Ala Val Gln Lys Arg His His Thr Arg Leu  
 610 615 620  
 Phe Ala Val Asp Lys Lys Asp Gln Val Gly Lys Ala Tyr Asn Ile Pro  
 625 630 635 640

Pro Gly Thr Thr Val Asp Val Gly Ile Thr His Pro Thr Glu Phe Asp  
 645 650 655  
 Phe Tyr Leu Cys Ser His Ala Gly Ile Gln Gly Thr Ser Arg Pro Ser  
 660 665 670  
 His Tyr His Val Leu Trp Asp Asp Asn Asn Leu Thr Ala Asp Glu Leu  
 675 680 685  
 Gln Gln Leu Thr Tyr Gln Met Cys His Thr Tyr Val Arg Cys Thr Arg  
 690 695 700  
 Ser Val Ser Ile Pro Ala Pro Ala Tyr Tyr Ala His Leu Val Ala Phe  
 705 710 715 720  
 Arg Ala Arg Tyr His Leu Val Asp Arg Glu His Asp Ser Gly Glu Gly  
 725 730 735  
 Ser Gln Pro Ser Gly Thr Ser Glu Asp Thr Thr Leu Ser Asn Met Ala  
 740 745 750  
 Arg Ala Val Gln Val Ile Leu Ala Phe Asn Leu Val Ser Ile  
 755 760 765

<210> 10

<211> 737

<212> PRT

<213> *Oryctolagus cuniculus*

<400> 10

Gly Lys Asp Arg Ile Phe Lys Val Ser Ile Lys Trp Val Ser Cys Val  
 1 5 10 15  
 Ser Leu Gln Ala Leu His Asp Ala Leu Ser Gly Arg Leu Pro Ser Val  
 20 25 30  
 Pro Phe Glu Thr Ile Gln Ala Leu Asp Val Val Met Arg His Leu Pro  
 35 40 45  
 Ser Met Arg Tyr Thr Pro Val Gly Arg Ser Phe Phe Thr Ala Ser Glu  
 50 55 60  
 Gly Cys Ser Asn Pro Leu Gly Gly Gly Arg Glu Val Trp Phe Gly Phe  
 65 70 75 80  
 His Gln Ser Val Arg Pro Ser Leu Trp Lys Met Met Leu Asn Ile Asp  
 85 90 95  
 Val Ser Ala Thr Ala Phe Tyr Lys Ala Gln Pro Val Ile Glu Phe Val  
 100 105 110  
 Cys Glu Val Leu Asp Phe Lys Ser Ile Glu Glu Gln Gln Lys Pro Leu  
 115 120 125  
 Thr Asp Ser Gln Arg Val Lys Phe Thr Lys Glu Ile Lys Gly Leu Lys  
 130 135 140  
 Val Glu Ile Thr His Cys Gly Gln Met Lys Arg Lys Tyr Arg Val Cys  
 145 150 155 160  
 Asn Val Thr Arg Arg Pro Ala Ser His Gln Thr Phe Pro Leu Gln Gln  
 165 170 175  
 Glu Ser Gly Gln Thr Val Glu Cys Thr Val Ala Gln Tyr Phe Lys Asp  
 180 185 190  
 Arg His Lys Leu Val Leu Arg Tyr Pro His Leu Pro Cys Leu Gln Val  
 195 200 205  
 Gly Gln Glu Gln Lys His Thr Tyr Leu Pro Leu Glu Val Cys Asn Ile  
 210 215 220  
 Val Ala Gly Gln Arg Cys Ile Lys Lys Leu Thr Asp Asn Gln Thr Ser  
 225 230 235 240  
 Thr Met Ile Arg Ala Thr Ala Arg Ser Ala Pro Asp Arg Gln Glu Glu  
 245 250 255  
 Ile Ser Lys Leu Met Arg Ser Ala Ser Phe Asn Thr Asp Pro Tyr Val  
 260 265 270

Arg Glu Phe Gly Ile Met Val Lys Asp Glu Met Thr Asp Val Thr Gly  
 275 280 285  
 Arg Val Leu Gln Pro Pro Ser Ile Leu Tyr Gly Gly Arg Asn Lys Ala  
 290 295 300  
 Ile Ala Thr Pro Val Gln Gly Val Trp Asp Met Arg Asn Lys Gln Phe  
 305 310 315 320  
 His Thr Gly Ile Glu Ile Lys Val Trp Ala Ile Ala Cys Phe Ala Pro  
 325 330 335  
 Gln Arg Gln Cys Thr Glu Val His Leu Lys Ser Phe Thr Glu Gln Leu  
 340 345 350  
 Arg Lys Ile Ser Arg Asp Ala Gly Met Pro Ile Gln Gly Gln Pro Cys  
 355 360 365  
 Phe Cys Lys Tyr Ala Gln Gly Ala Asp Ser Val Gly Pro Met Phe Arg  
 370 375 380  
 His Leu Lys Asn Thr Tyr Ala Gly Leu Gln Leu Val Val Val Ile Leu  
 385 390 395 400  
 Pro Gly Lys Thr Pro Val Tyr Ala Glu Val Lys Arg Val Gly Asp Thr  
 405 410 415  
 Val Leu Gly Met Ala Thr Gln Cys Val Gln Met Lys Asn Val Gln Arg  
 420 425 430  
 Thr Thr Pro Gln Thr Leu Ser Asn Leu Cys Leu Lys Ile Asn Val Lys  
 435 440 445  
 Leu Gly Gly Val Asn Asn Ile Leu Leu Pro Gln Gly Arg Pro Pro Val  
 450 455 460  
 Phe Gln Gln Pro Val Ile Phe Leu Gly Ala Asp Val Thr His Pro Pro  
 465 470 475 480  
 Ala Gly Asp Gly Lys Lys Pro Ser Ile Ala Ala Val Val Gly Ser Met  
 485 490 495  
 Asp Ala His Pro Asn Arg Tyr Cys Ala Thr Val Arg Val Gln Gln His  
 500 505 510  
 Arg Gln Glu Ile Ile Gln Asp Leu Ala Ala Met Val Arg Glu Leu Leu  
 515 520 525  
 Ile Gln Phe Tyr Lys Ser Thr Arg Phe Lys Pro Thr Arg Ile Ile Phe  
 530 535 540  
 Tyr Arg Asp Gly Val Ser Glu Gly Gln Phe Gln Gln Val Leu His His  
 545 550 555 560  
 Glu Leu Leu Ala Ile Arg Glu Ala Cys Ile Lys Leu Glu Lys Asp Tyr  
 565 570 575  
 Gln Pro Gly Ile Thr Phe Ile Val Val Gln Lys Arg His His Thr Arg  
 580 585 590  
 Leu Phe Cys Thr Asp Lys Asn Glu Arg Val Gly Lys Ser Gly Asn Ile  
 595 600 605  
 Pro Ala Gly Thr Thr Val Asp Thr Lys Ile Thr His Pro Thr Glu Phe  
 610 615 620  
 Asp Phe Tyr Leu Cys Ser His Ala Gly Ile Gln Gly Thr Ser Arg Pro  
 625 630 635 640  
 Ser His Tyr His Val Leu Trp Asp Asp Asn Arg Phe Ser Ser Asp Glu  
 645 650 655  
 Leu Gln Ile Leu Thr Tyr Gln Leu Cys His Thr Tyr Val Arg Cys Thr  
 660 665 670  
 Arg Ser Val Ser Ile Pro Ala Pro Ala Tyr Tyr Ala His Leu Val Ala  
 675 680 685  
 Phe Arg Ala Arg Tyr His Leu Val Asp Lys Glu His Asp Ser Ala Glu  
 690 695 700  
 Gly Ser His Thr Ser Gly Gln Ser Asn Gly Arg Asp His Gln Ala Leu  
 705 710 715 720

Ala Lys Ala Val Gln Val His Gln Asp Thr Leu Arg Thr Met Tyr Phe  
 725 730 735  
 Ala

<210> 11  
 <211> 298  
 <212> PRT  
 <213> *Xenopus laevis*

<400> 11  
 Met Ser Ser Glu Lys Pro Thr Ser Leu Asn Ala Met Arg Ala Thr Asn  
 1 5 10 15  
 Pro Cys Glu Thr Pro Ile Gln Leu Leu His Glu Phe Gly Thr Lys Thr  
 20 25 30  
 Gly Asn His Pro Val Tyr Thr Leu Glu Lys Ala Glu Gly Gln Ala His  
 35 40 45  
 Asn Pro Ser Phe Thr Phe Arg Leu Val Ile Gly Asp Ile Thr Ser Leu  
 50 55 60  
 Gly Glu Gly Pro Ser Lys Lys Thr Pro Lys Gln Lys Ala Ala Glu Phe  
 65 70 75 80  
 Ala Leu Asn Ile Leu Arg Gly Asp Thr Ser Lys Cys Leu Pro Val Thr  
 85 90 95  
 Asp Thr Leu Arg Asp Pro Lys Lys Pro Pro Asn Gln Met Gln Glu Asn  
 100 105 110  
 Pro Val Gly Ser Leu Gln Glu Leu Ala Val Gln Lys Gly Trp Arg Leu  
 115 120 125  
 Pro Glu Tyr Thr Val Ala Gln Glu Ser Gly Pro Pro His Lys Arg Glu  
 130 135 140  
 Phe Thr Ile Thr Cys Arg Val Glu Thr Phe Val Glu Thr Gly Ser Gly  
 145 150 155 160  
 Thr Ser Lys Gln Val Ala Lys Arg Val Ala Ala Glu Lys Leu Leu Thr  
 165 170 175  
 Lys Phe Lys Thr Ile Ser Thr Asp Asn Ile Pro Leu Asn Lys Leu Ile  
 180 185 190  
 Gly Asn Lys Met Gly Cys Thr Trp Asp Ser Met Arg Asn Ser Ser Gly  
 195 200 205  
 Glu Lys Ile Ser Met Leu Lys Arg Ser Pro Leu Ser Ile Pro Asn Thr  
 210 215 220  
 Asp Tyr Val Lys Met Leu Lys Asp Val Ala Glu Glu Leu Asp Phe Asn  
 225 230 235 240  
 Leu Thr Tyr Leu Asp Ile Asp Glu Leu Ser Val Asn Gly Gln Tyr Gln  
 245 250 255  
 Cys Leu Ala Glu Leu Ser Thr Asn Pro Ile Thr Val Cys His Gly Thr  
 260 265 270  
 Gly Ile Ser Cys Gly Asn Ala His Asn Asp Ala Ala His Asn Ala Leu  
 275 280 285  
 Gln Tyr Leu Lys Ile Met Cys Ile Lys Lys  
 290 295

<210> 12  
 <211> 551  
 <212> PRT  
 <213> *Homo sapiens*

<220>  
 <221> VARIANT



&lt;222&gt; (1)...(551)

&lt;223&gt; Xaa = Any Amino Acid

&lt;400&gt; 12

Met Ala Gly Asp Leu Ser Ala Gly Phe Phe Met Glu Glu Leu Asn Thr  
 1 5 10 15  
 Tyr Arg Gln Lys Gln Gly Val Val Leu Lys Tyr Gln Glu Leu Pro Asn  
 20 25 30  
 Ser Gly Pro Pro His Asp Arg Arg Phe Thr Phe Gln Val Ile Ile Asp  
 35 40 45  
 Gly Arg Glu Phe Pro Glu Gly Glu Gly Arg Ser Lys Lys Glu Ala Xaa  
 50 55 60  
 Asn Ala Ala Ala Xaa Leu Ala Val Glu Ile Leu Asn Lys Glu Lys Lys  
 65 70 75 80  
 Ala Val Ser Pro Leu Leu Leu Thr Thr Thr Asn Ser Ser Glu Gly Leu  
 85 90 95  
 Ser Met Gly Asn Tyr Ile Gly Leu Ile Asn Arg Ile Ala Gln Lys Lys  
 100 105 110  
 Arg Leu Thr Val Asn Tyr Glu Gln Cys Ala Ser Gly Val His Gly Pro  
 115 120 125  
 Glu Gly Phe His Tyr Lys Cys Lys Met Gly Gln Lys Glu Tyr Ser Ile  
 130 135 140  
 Gly Thr Gly Ser Thr Lys Gln Glu Ala Lys Gln Leu Ala Ala Lys Leu  
 145 150 155 160  
 Ala Tyr Leu Gln Ile Leu Ser Glu Glu Thr Ser Val Lys Ser Asp Tyr  
 165 170 175  
 Leu Ser Ser Gly Ser Phe Ala Thr Thr Cys Glu Ser Gln Ser Asn Ser  
 180 185 190  
 Leu Val Thr Ser Thr Leu Ala Ser Glu Ser Ser Ser Glu Gly Asp Phe  
 195 200 205  
 Ser Ala Asp Thr Ser Glu Ile Asn Ser Asn Ser Asp Ser Leu Asn Ser  
 210 215 220  
 Ser Ser Leu Leu Met Asn Gly Leu Arg Asn Asn Gln Arg Lys Ala Lys  
 225 230 235 240  
 Arg Ser Leu Ala Pro Arg Phe Asp Leu Pro Asp Met Lys Glu Thr Lys  
 245 250 255  
 Tyr Thr Val Asp Lys Arg Phe Gly Met Asp Phe Lys Glu Ile Glu Leu  
 260 265 270  
 Ile Gly Ser Gly Gly Phe Gly Gln Val Phe Lys Ala Lys His Arg Ile  
 275 280 285  
 Asp Gly Lys Thr Tyr Val Ile Lys Arg Val Lys Tyr Asn Asn Glu Lys  
 290 295 300  
 Ala Glu Arg Glu Val Lys Ala Leu Ala Lys Leu Asp His Val Asn Ile  
 305 310 315 320  
 Val His Tyr Asn Gly Cys Trp Asp Gly Phe Asp Tyr Asp Pro Glu Thr  
 325 330 335  
 Ser Asp Asp Ser Leu Glu Ser Ser Asp Tyr Asp Pro Glu Asn Ser Lys  
 340 345 350  
 Asn Ser Ser Arg Ser Lys Thr Lys Cys Leu Phe Ile Gln Met Glu Phe  
 355 360 365  
 Cys Asp Lys Gly Thr Leu Glu Gln Trp Ile Glu Lys Arg Arg Gly Glu  
 370 375 380  
 Lys Leu Asp Lys Val Leu Ala Leu Glu Leu Phe Glu Gln Ile Thr Lys  
 385 390 395 400  
 Gly Val Asp Tyr Ile His Ser Lys Lys Leu Ile His Arg Asp Leu Lys  
 405 410 415

Pro Ser Asn Ile Phe Leu Val Asp Thr Lys Gln Val Lys Ile Gly Asp  
 420 425 430  
 Phe Gly Leu Val Thr Ser Leu Lys Asn Asp Gly Lys Arg Thr Arg Ser  
 435 440 445  
 Lys Gly Thr Leu Arg Tyr Met Ser Pro Glu Gln Ile Ser Ser Gln Asp  
 450 455 460  
 Tyr Gly Lys Glu Val Asp Leu Tyr Ala Leu Gly Leu Ile Leu Ala Glu  
 465 470 475 480  
 Leu Leu His Val Cys Asp Thr Ala Phe Glu Thr Ser Lys Phe Phe Thr  
 485 490 495  
 Asp Leu Arg Asp Gly Ile Ile Ser Asp Ile Xaa Asp Lys Lys Glu Glu  
 500 505 510  
 Thr Leu Leu Gln Lys Leu Leu Ser Lys Xaa Pro Glu Asp Arg Pro Asn  
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 530 535 540  
 Lys Asn Glu Arg His Thr Cys  
 545 550

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 <212> PRT  
 <213> Caenorhabditis elegans

<400> 13  
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 Phe Glu Gln Ser Leu Glu Val Ala Pro Arg Ile Glu Ala Trp Phe Gly  
 35 40 45  
 Ile Tyr Ile Gly Ile Lys Glu Leu Phe Asp Gly Glu Pro Val Leu Asn  
 50 55 60  
 Phe Ala Ile Val Asp Lys Leu Phe Tyr Asn Ala Pro Lys Met Ser Leu  
 65 70 75 80  
 Leu Asp Tyr Leu Leu Leu Ile Val Asp Pro Gln Ser Cys Asn Asp Asp  
 85 90 95  
 Val Arg Lys Asp Leu Lys Thr Lys Leu Met Ala Gly Lys Met Thr Ile  
 100 105 110  
 Arg Gln Ala Ala Arg Pro Arg Ile Arg Gln Leu Leu Glu Asn Leu Lys  
 115 120 125  
 Leu Lys Cys Ala Glu Val Trp Asp Asn Glu Met Ser Arg Leu Thr Glu  
 130 135 140  
 Arg His Leu Thr Phe Leu Asp Leu Cys Glu Glu Asn Ser Leu Val Tyr  
 145 150 155 160  
 Lys Val Thr Gly Lys Ser Asp Arg Gly Arg Asn Ala Lys Lys Tyr Asp  
 165 170 175  
 Thr Thr Leu Phe Lys Ile Tyr Glu Glu Asn Lys Lys Phe Ile Glu Phe  
 180 185 190  
 Pro His Leu Pro Leu Val Lys Val Lys Ser Gly Ala Lys Glu Tyr Ala  
 195 200 205  
 Val Pro Met Glu His Leu Glu Val His Glu Lys Pro Gln Arg Tyr Lys  
 210 215 220  
 Asn Arg Ile Asp Leu Val Met Gln Asp Lys Phe Leu Lys Arg Ala Thr  
 225 230 235 240  
 Arg Lys Pro His Asp Tyr Lys Glu Asn Thr Leu Lys Met Leu Lys Glu  
 245 250 255

Leu Asp Phe Ser Ser Glu Glu Leu Asn Phe Val Glu Arg Phe Gly Leu  
 260 265 270  
 Cys Ser Lys Leu Gln Met Ile Glu Cys Pro Gly Lys Val Leu Lys Glu  
 275 280 285  
 Pro Met Leu Val Asn Ser Val Asn Glu Gln Ile Lys Met Thr Pro Val  
 290 295 300  
 Ile Arg Gly Phe Gln Glu Lys Gln Leu Asn Val Val Pro Glu Lys Glu  
 305 310 315 320  
 Leu Cys Cys Ala Val Phe Val Val Asn Glu Thr Ala Gly Asn Pro Cys  
 325 330 335  
 Leu Glu Glu Asn Asp Val Val Lys Phe Tyr Thr Glu Leu Ile Gly Gly  
 340 345 350  
 Cys Lys Phe Arg Gly Ile Arg Ile Gly Ala Asn Glu Asn Arg Gly Ala  
 355 360 365  
 Gln Ser Ile Met Tyr Asp Ala Thr Lys Asn Glu Tyr Ala Phe Tyr Lys  
 370 375 380  
 Asn Cys Thr Leu Asn Thr Gly Ile Gly Arg Phe Glu Ile Ala Ala Thr  
 385 390 395 400  
 Glu Ala Lys Asn Met Phe Glu Arg Leu Pro Asp Lys Glu Gln Lys Val  
 405 410 415  
 Leu Met Phe Ile Ile Ile Ser Lys Arg Gln Leu Asn Ala Tyr Gly Phe  
 420 425 430  
 Val Lys His Tyr Cys Asp His Thr Ile Gly Val Ala Asn Gln His Ile  
 435 440 445  
 Thr Ser Glu Thr Val Thr Lys Ala Leu Ala Ser Leu Arg His Glu Lys  
 450 455 460  
 Gly Ser Lys Arg Ile Phe Tyr Gln Ile Ala Leu Lys Ile Asn Ala Lys  
 465 470 475 480  
 Leu Gly Gly Ile Asn Gln Glu Leu Asp Trp Ser Glu Ile Ala Glu Ile  
 485 490 495  
 Ser Pro Glu Glu Lys Glu Arg Arg Lys Thr Met Pro Leu Thr Met Tyr  
 500 505 510  
 Val Gly Ile Asp Val Thr His Pro Thr Ser Tyr Ser Gly Ile Asp Tyr  
 515 520 525  
 Ser Ile Ala Ala Val Val Ala Ser Ile Asn Pro Gly Gly Thr Ile Tyr  
 530 535 540  
 Arg Asn Met Ile Val Thr Gln Glu Glu Cys Arg Pro Gly Glu Arg Ala  
 545 550 555 560  
 Val Ala His Gly Arg Glu Arg Thr Asp Ile Leu Glu Ala Lys Phe Val  
 565 570 575  
 Lys Leu Leu Arg Glu Phe Ala Glu Asn Asn Asp Asn Arg Ala Pro Ala  
 580 585 590  
 His Ile Val Val Tyr Arg Asp Gly Val Ser Asp Ser Glu Met Leu Arg  
 595 600 605  
 Val Ser His Asp Glu Leu Arg Ser Leu Lys Ser Glu Val Lys Gln Phe  
 610 615 620  
 Met Ser Glu Arg Asp Gly Glu Asp Pro Glu Pro Lys Tyr Thr Phe Ile  
 625 630 635 640  
 Val Ile Gln Lys Arg His Asn Thr Arg Leu Leu Arg Arg Met Glu Lys  
 645 650 655  
 Asp Lys Pro Val Val Asn Lys Asp Leu Thr Pro Ala Glu Thr Asp Val  
 660 665 670  
 Ala Val Ala Ala Val Lys Gln Trp Glu Glu Asp Met Lys Glu Ser Lys  
 675 680 685  
 Glu Thr Gly Ile Val Asn Pro Ser Ser Gly Thr Thr Val Asp Lys Leu  
 690 695 700

Ile Val Ser Lys Tyr Lys Phe Asp Phe Phe Leu Ala Ser His His Gly  
 705 710 715 720  
 Val Leu Gly Thr Ser Arg Pro Gly His Tyr Thr Val Met Tyr Asp Asp  
 725 730 735  
 Lys Gly Met Ser Gln Asp Glu Val Tyr Lys Met Thr Tyr Gly Leu Ala  
 740 745 750  
 Phe Leu Ser Ala Arg Cys Arg Lys Pro Ile Ser Leu Pro Val Pro Val  
 755 760 765  
 His Tyr Ala His Leu Ser Cys Glu Lys Ala Lys Glu Leu Tyr Arg Thr  
 770 775 780  
 Tyr Lys Glu His Tyr Ile Gly Asp Tyr Ala Gln Pro Arg Thr Arg His  
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 805 810 815  
 Phe Ala

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 <213> Caenorhabditis elegans

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 20 25 30  
 Ile Cys Thr Met Cys Asn Gln Lys Thr Arg Gly Ile Thr Ser Lys Gln  
 35 40 45  
 Lys Asp Ala Lys Asn Leu Ala Ala Trp Leu Met Trp Lys Ala Leu  
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<220>  
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<400> 15  
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